



Docket No: 10738-29

PATENT

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicants: Sharp, Frank R. et al

Serial No.: 09/996,275

Group Art Unit: 1637

Filed: Nov. 28, 2001

Examiner: Jeffrey N. Fredman

For: **Blood Assessment of Injury**

RESPONSE TO RESTRICTION REQUIREMENT

10 Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

15 Dear Sir:

In the Official Action dated June 6, 2005, the Examiner required multiple elections and a further restriction under 35 U.S.C. §§ 121. In **Election 1**, the Examiner requires election of a single disease for examination, asserting that examining each species would be extremely burdensome since each disease is multifactorial and would require separate analyses for enablement and prior art. The Examiner required election of a single disclosed species for prosecution, to which the claims will be restricted if no generic claims is finally held allowable. The Examiner further asserts that currently there is no claim generic to the entire invention. The Examiner points specifically to claim 70, for example, as being drawn to immune mediated disease and not to injury, as required by claim 1." In addition to the election of a species, the Examiner requests a listing of all claims readable thereon. This election requirement is traversed and reconsideration is respectfully requested.

Applicants submit that the Examiner has misconstrued the invention in coming to the conclusion that it would be burdensome, absent this election, to search several multifactorial diseases. The present invention is directed to methods of assessing injury. Applicants point out that, as defined in the present specification, "disease" is merely a subset of the category "injury." (See, for example, the definition of "injury" in the Field of the Invention on page 1, lines 11-13: "injury" is defined "where there is an isolated dysfunction or isolated loss of neurons or individual cells in the blood, brain, spinal cord, lung, muscles, nerves or other organs.") Applicants concur that this is not a definition of "injury" that comports precisely with common usage of the term, but, as defined by Applicants it is a generic category to which all the recited diseases and conditions belong. Indeed, claim 70, specifically mentioned by the Examiner as not being a subset or species of "injury," is directed to a method of immune mediated disease assessment in an individual comprising, inter alia, (d) comparing the pattern of expression to an injury database to assess immune mediated disease. Hence, on its face, this claim makes it clear that the Applicants consider disease to constitute a subset of injury.

Throughout the specification and claims, databases described as specific disease databases are recited as dependent from the generic "injury database." For example, claim 20 recites an injury database comprising, inter alia, a disease specific injury database. Claims 25-37 are all directed to disease specific databases and all depend from claim 1 and limit the recitation of an injury database. Independent claims 38, 43, 47, 51, 56, 63, 66, 70, 74, 77, 82, 86, and 90 are all directed to methods of specific disease assessment comprising, inter alia, comparing the pattern of expression to an injury database to the specific disease state. In other words, once it is understood, as taught by the present invention, that all the recited disease states are subsets of "injury" as recited in claim 1, it becomes clear that claim 1 is in fact a generic claim.

Further, there would be no enablement issue on a disease state by disease state basis, for if claim 1 is enabled, then, according to the present definition of "injury," then the more specific embodiments are likewise enabled as they all constitute the "injury" of the generic claim.

Provisionally, however, Applicants elect, with traverse, to prosecute the
60 species recited in claim 29, directed to the method of claim 1 wherein the injury
assessment comprises stroke injury assessment. The claims readable thereon include
claims 1-22, 29 and claims 38-42.

In Election 2, the Examiner requires election of a single microarray type,
specifically to either a protein-based or nucleic acid-based method. The Examiner
65 asserts that the search and examination of each of these would be burdensome
"because they are independent and distinct compounds which share no structural
homology and for which different search terms and different prior art would be
applicable." This election requirement is traversed and reconsideration is respectfully
requested.

Applicants note that it is not the proteins or nucleic acids themselves, in the
abstract, that are relevant to the present claims. Rather, it is a pattern of expression.
For example, one need not inspect, analyze or otherwise consider individual nucleic
acids or proteins, except to the extent it is necessary to discern a pattern as presently
taught. Further, the expression pattern at issue in all the present embodiments is
75 exhibited by a blood sample. The dependent claims which recite the options of gene
expression, protein expression, or combinations thereof for each independent method
claim simply acknowledge that different databases may be available for different
specific injuries, or may be more or less comprehensive depending on the specific
disease state. Thus, according to the dependent claims directed to methods wherein
80 the pattern of expression comprises gene expression protein expression, or
combinations thereof, one of which exists for each specific disease injury
embodiment, the practitioner is provided with options which are suitable with respect
to the database available or most comprehensive.

Provisionally, however, Applicants elect a nucleic-acid based microarray
85 method.

In a further Restriction Requirement, the Examiner requested election of a
specific sequence or gene as recited in Tables 2 or 3. Although the Examiner
explicitly refers to this request by "Applicant is required to further elect.." the
Examiner states that this is not an election of species. The Examiner notes that each

90 nucleotide sequence is presumed to represent an independent and distinct invention subject to restriction requirement pursuant to 35 U.S.C. 121. The Examiner asserts that because the "inventions" have different classifications and divergent subject matter, examination would pose a serious burden and restriction is therefore proper.

Applicants must respectfully traverse and are in the quandary of being unable
95 to make a provisional election as requested by the Examiner, without deviating from the essential nature of the instant invention. The present invention recognizes and exploits patterns of expression in methods of assessing injuries. The Examiner, on the other hand is requesting restriction to a single gene. As explained in the present specification, the present invention assesses injury by reference to expression patterns,
100 not functioning of a single gene. Down or up regulation of a single gene is not relevant out of context and cannot define a "pattern" within the meaning of the claims.

Applicants point to page 42 to explain the data in Tables 2-3. That is, the data illustrates that patterns of expression in the blood are unique for stroke, hypoxia and status epilepticus as compared with sham controls. Since the pattern of expression is
105 different for each injury subtype, the pattern can be used to assess the injury. The basis, as noted in the specification, is that gene expression in the blood differs following different types of injury in a way that permits injury assessment (page 43, lines 6-7 e.g.).

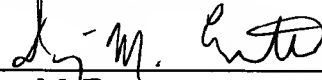
The patterns comprise data points with each data point provided by
110 determination of a gene expression product in a blood sample. A single data point does not provide relevant or sufficient information. The invention is not directed to specific genes or expression products thereof. In fact, the genes providing the data points are already in the public domain and the Applicants do not assert their novelty or patentability. The invention encompasses methods. The methods utilize
115 expression patterns in blood to assess injury. It is not possible for Applicants to elect a "specific sequence or gene as recited in Tables 2 or 3" as requested by the Examiner.

In an effort to clarify the both the subject matter of the claims and the gist of the restriction request, Applicants called the Examiner. The Examiner responded with a telephone message stating that this restriction requirement was not intended to be
120 applied to the sequences referred to in the tables, and that restriction between the

listings in the Tables was not being requested. Since this appears to be the only restriction basis asserted, Applicants assume that the Examiner has reconsidered.

Respectfully submitted,

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